

## KPC-2-Producing Sequence Type 11 *Klebsiella pneumoniae* Detected in Taiwan

In Taiwan, the majority of carbapenem-resistant *Enterobacteriaceae* (CRE) isolates exhibited low-level carbapenem resistance, and with the exception of a few isolates with VIM or IMP-8 carbapenemase (6, 7, 13), most were due to the production of extended spectrum  $\beta$ -lactamase (ESBL) and/or AmpC  $\beta$ -lactamase plus outer membrane protein porin loss (2, 7, 14). To date, there has been only one case of *Klebsiella pneumoniae* carbapenemase (KPC)-producing *K. pneumoniae* reported in Taiwan from a patient who was hospitalized in China prior to being transferred back to Taiwan. The isolate harbored KPC-2, but the genetic background of the strain was not mentioned (3).

We report the detection of four KPC-2-positive *K. pneumoniae* isolates from two patients in another hospital in Taiwan. Patient A was a 74-year-old Taiwanese male who was hospitalized in China for emergency medical treatment due to sudden cardiac arrest in 2010. He was transferred back to the coronary care unit (CCU) of a Taiwanese hospital 5 days later. He developed urinary tract infection due to a carbapenem-resistant *K. pneumoniae* (CRKP) isolate (CRKP1) 5 days after being admitted to the CCU. Two additional CRKP isolates were recovered from the central venous catheter (CRKP3) and from urine (CRKP4) 5 weeks after admission. Unfortunately, he expired due to the occurrence of hepatoma rupture and shock. Patient B was an 87-year-old Taiwanese male who was hospitalized in the same CCU because of congestive heart failure during the same period. He developed pneumonia, and CRKP isolates were recovered from the central venous catheter tip and from a sputum specimen 1 day apart. Only his sputum isolate (CRKP2) was available for further workup. CRKP2 was isolated 19 days after CRKP1. Patient B later accepted hospice care due to the terminal stage of congestive heart failure.

The pulsed-field gel electrophoresis (PFGE) patterns of CRKP1 to CRKP4 isolates were indistinguishable (data not shown). All four isolates had the same antibiogram and were resistant to all tested  $\beta$ -lactams (Table 1), with high ertapenem, imipenem, and meropenem MICs ( $\geq 32$   $\mu\text{g/ml}$ ), and susceptible only to polymyxin B, tigecycline, and trimethoprim-sulfamethoxazole. All four were positive for *bla*<sub>KPC-2</sub>, as well as *bla*<sub>SHV-12</sub> and *bla*<sub>CTX-M</sub>, and belong to sequence type 11 (ST11) (allelic profile 3-3-1-1-1-4) (5, 8, 9, 11). The plasmids of CRKP1 and CRKP2 were introduced into *Escherichia coli* DH10B by electroporation. The pCRKP1/DH10B and pCRKP2/DH10B electrotransformants became resistant to all tested  $\beta$ -lactams (Table 1), including carbapenems (MICs of 12 to  $>32$   $\mu\text{g/ml}$ ), and were positive for *bla*<sub>KPC-2</sub> and *bla*<sub>SHV-12</sub> but not *bla*<sub>CTX-M</sub>. Restriction fingerprinting patterns of plasmid DNAs from the transformants were similar (Fig. 1).

In Asia, KPC-producing *K. pneumoniae* was first detected in a 2004 isolate from China (12), where KPC-2-producing *Enterobacteriaceae* bacteria were subsequently disseminated in different regions (1, 10, 15). ST11 was found to be the predominant KPC-2-producing *K. pneumoniae* sequence type isolated from multiple cities of China (10). Those ST11 isolates also

TABLE 1 MICs of four KPC-2-positive carbapenem-resistant *Klebsiella pneumoniae* clinical strains (CRKP1 to CRKP4), *Escherichia coli* DH10B electrotransformants, and DH10B

| Antimicrobial agent        | MIC ( $\mu\text{g/ml}$ ) of each strain or group of strains <sup>a</sup> |   |                                      |
|----------------------------|--|---|--------------------------------------|
|                            | <i>K. pneumoniae</i><br>CRKP1 to<br>CRKP4 <sup>b</sup>                   | Electrotransformants<br>of DH10B <sup>c</sup> | <i>E. coli</i><br>DH10B <sup>d</sup> |
| Amikacin                   | >128   | 2   | 2                                    |
| Ampicillin                 | >256   | >256  | 4                                    |
| Aztreonam                  | >256   | >256  | 0.19                                 |
| Cefepime                   | 256  | >256  | 0.064                                |
| Cefotaxime                 | >256   | >256  | 0.125                                |
| Cefoxitin                  | >256   | 96  | 6                                    |
| Ceftazidime                | >256   | >256  | 0.38                                 |
| Cefuroxime                 | >256   | >256  | 4                                    |
| Ceftriaxone                | >256   | >256  | 0.094                                |
| Ciprofloxacin              | >32  | 0.004   | 0.004                                |
| Ertapenem                  | >32  | 32  | 0.008                                |
| Fosfomycin                 | 128  | 1   | 1                                    |
| Gentamicin                 | >128   | 0.75  | 0.5                                  |
| Imipenem                   | 32   | 32  | 0.25                                 |
| Meropenem                  | >32  | 12-24   | 0.032                                |
| Piperacillin-tazobactam    | >256   | >256  | 2                                    |
| Polymyxin B                | 1.5  | 0.5   | 0.19                                 |
| Tigecycline                | 1.0-1.5  | 0.25  | 0.19                                 |
| TMP/SMX (SXT) <sup>e</sup> | 0.5  | 0.047   | 0.047                                |

<sup>a</sup> MIC data shown are from Etest. All agents except fosfomycin were also tested by a broth microdilution method (4).

<sup>b</sup> In *K. pneumoniae* CRKP1 to CRKP4, genes encoding SHV-12- and CTX-M-type ESBLs were detected, no AmpC  $\beta$ -lactamase genes were detected, the KPC-2 carbapenemase gene was detected, and the modified Hodge test (MHT) was positive with ertapenem.

<sup>c</sup> pCRKP1/DH10B and pCRKP2/DH10B electrotransformants. In these electrotransformants, the gene encoding SHV-12 ESBL was detected, no AmpC  $\beta$ -lactamase genes were detected, the KPC-2 carbapenemase gene was detected, and the modified Hodge test (MHT) was positive with ertapenem.

<sup>d</sup> In *E. coli* DH10B, no ESBL, AmpC  $\beta$ -lactamase, and carbapenemase genes were detected, and the modified Hodge test (MHT) with ertapenem was negative.

<sup>e</sup> TMP-SMX (SXT), trimethoprim-sulfamethoxazole.

carried a combination of SHV-type and CTX-M-type ESBLs and AmpC  $\beta$ -lactamases (10).

It is possible that patient A acquired KPC-producing *K. pneumoniae* during his hospitalization in China and that the strain was then transmitted to patient B in the same ward in Taiwan. Although the prevalence of carbapenem-resistant *Enterobacteriaceae* in Taiwan has remained low (2, 7, 14), the emergence of KPC-producing *K. pneumoniae* is worrisome since multidrug-resistant *Enterobacteriaceae* bacteria are already prevalent in Taiwan, neces-

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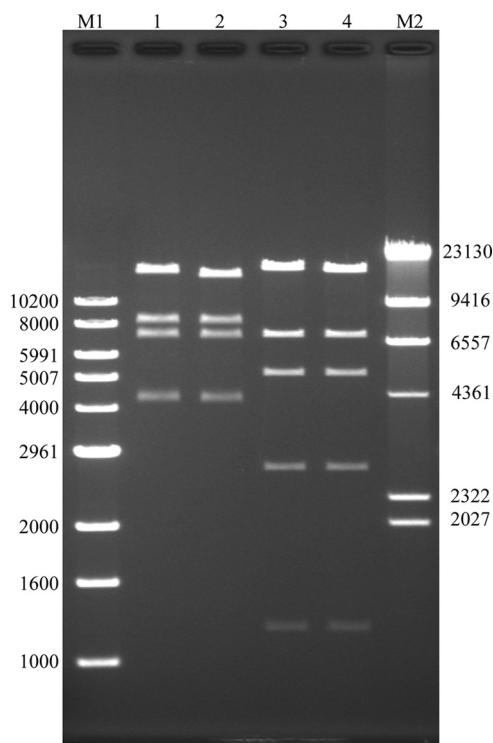


FIG 1 BglIII (lanes 1 and 2) and SacI (lanes 3 and 4) restriction digest of plasmid DNAs from *E. coli* DH10B electrotransformants. M1, 1-kb DNA ladder (numbers are bp); lanes 1 and 3, pCRKP1/DH10B; lanes 2 and 4, pCRKP2/DH10B. CRKP1 and CRKP2 were isolated from 2 patients of the same ward 19 days apart. M2,  $\lambda$ /HindIII ladder.

sitating increased carbapenem use. Careful monitoring systems need to be implemented and should include patients transferred from hospitals abroad.

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